



UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/030,605	05/31/2002	Ulrike Fiedler	1406/37	8368
25297 7590 11/16/2007 JENKINS, WILSON, TAYLOR & HUNT, P. A. 3100 TOWER BLVD., Suite 1200 DURHAM, NC 27707			EXAMINER BORIN, MICHAEL L	
			ART UNIT 1631	PAPER NUMBER
			MAIL DATE 11/16/2007	DELIVERY MODE PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/030,605	FIEDLER ET AL.	
	Examiner	Art Unit	
	Michael Borin	1631	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 08/28/2007.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 5-7,9-12,14-16,26-28,42 and 47 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 5-7,9-11,14,16,26-28,42 and 47 is/are rejected.
- 7) ☒ Claim(s) 12 and 15 is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

Art Unit: 1631

DETAILED ACTION

Status of Claims

1. Amendment filed 08/28/2007 is acknowledged. Claims 1-4, 8,13,17-25,29-41,43-46 are canceled. Claim 47 is added. Claims 5-7,9-12,14-16,26-28,42,47 are pending.

Claim Rejections - 35 USC 112, first paragraph (written description).

The following rejection is modified in view of applicant's comments and amendments to the claims.

2. (Written Description) Claims 5-7,9-11,14,16,26-28,42,47 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention.

The breadth of the claims encompasses any gamma-crystallin polypeptide mutagenized at two, or three or four of beta strands of at least one beta sheet (there are four beta sheets in gamma crystallin) such that the mutant possesses a new binding activity which did not exist in the parent protein.

Art Unit: 1631

The claimed genus of mutant proteins is represented by two mutants of gamma-II-crystalline of SEQ ID No. 22 having the same seven residue-mutation of residues K3,T5,Y7,C16,E18,S20,D39 into R3,K5,K7,Y16,S18,N20,L39. This mutation takes place in, specifically, the first three beta strands of the first (from N-terminal end) beta sheet of gamma-crystallin. Only this mutation results in acquiring "a new binding activity"; there are no indication that the applicant was in possession of any other gamma-crystallin polypeptide of the broad genus as claimed which possessed a new binding activity as well. The above mutants, having very particular substitutions, are not sufficiently representative of the genus of any mutants of proteins encompassed by the claims; they are not sufficient to reasonably convey to one skilled in the relevant art that the inventors had possession of the entire genus of the mutants as claimed. For example, specification does not convey that applicants were in possession of mutant gamma-crystallin polypeptide demonstrating "a new binding activity" wherein the mutant has mutations in two, or four strands, in any other of "at least one beta-sheet", in any other substitutions than described for the above mutants, for any random combination of insertion, deletion, substitution, etc.

Further, the claimed mutants are addressed as having a functional limitation of having "a new binding activity" towards a[ny] binding partner. The only binding partner disclosed for the mutants addressed above is BSA-estradiol-17-hemisuccinate. The generally stated functional limitation of having "a new binding activity" towards any binding partner does not provide sufficient structural characteristics to define the genus

Art Unit: 1631

of the claimed proteins. Note, that the claims are directed to products, not to a method of making.

The inventor must be able to describe the item to be patented with such clarity that the reader is assured that the inventor actually has possession and knowledge of the unique method that makes it worthy of patent protection. The reader can certainly appreciate the goal but establishing goals does not make a patent. As the Court of Appeals for the Federal Circuit stated in a case involving similar issues, an inadequate patent description that merely identifies a plan to accomplish an intended result "is an attempt to preempt the future before it has arrived." *Fiers v. Revel*, 984 F.2d 1164, 1171 (Fed. Cir.1993). To satisfy the written-description requirement, the specification must describe every element of the claimed invention in sufficient detail so that one of ordinary skill in the art would recognize that the inventor possessed the claimed invention at the time of filing. *Vas-Cath*, 935 F.3d at 1563; see also *Lockwood v. American Airlines, Inc.*, 107 F.3d 1565, 1572 (Fed. Cir. 1997) (patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention"). There is no demonstration in the specification that besides one very specific mutant containing mutations at seven particular locations of bovine gamma II crystallin and having binding affinity for particular binding agent, BSA-estradiol-17-hemisuccinate, applicants generated any other crystalline protein having new characteristics other than ability to bind BSA-estradiol-17-hemisuccinate. Much less there is any demonstration in the specification of any other

Art Unit: 1631

protein which, being mutagenized, appropriated new functional characteristics as claimed.

Response to arguments

Applicant argues that "Considering the high degree of conservation in crystallins during evolution, the skilled artisan would have no difficulties in applying the principles disclosed in the instant specification to other gamma-crystallins." (p. 15 of the response). However, the point of the rejection is not only that there is no sufficient written description demonstrating possession of mutants of other species of gamma-crystallins, but, more importantly, lack of description of possession of genus of mutants of gamma-crystallin polypeptides demonstrating "a new binding activity". For example, specification does not convey that applicants were in possession of mutant gamma-crystallin polypeptide demonstrating "a new binding activity" wherein the mutant has mutations in two, or four strands, in any other of "at least one beta-sheet", in any other substitutions than described for the above mutants, in three beta strands of two antiparallel beta sheets, for any random combination of insertion, deletion, substitution, etc.

Claim Rejections - 35 USC § 112, first paragraph (enablement).

3. Claims 5-7,9,11,14,16,26-28,42,47 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for mutants of bovine gamma crystallin of SEQ ID No. 22 obtained by mutations at positions identified in claim

Art Unit: 1631

12, does not reasonably provide enablement for mutants of other crystallins, much less for other proteins with mutations at beta sheet structure as claimed.

The rejection is maintained for the reasons of record and further in view of the following.

Response to arguments

First, applicant argues that "the specification provides substantial guidance as to locations of the mutations" and points at page 9. However, said section of specification does not address gamma-crystallin and addresses any protein with beta-strand structures. Further, applicant, in the same paragraph of the arguments submits that it is not any beta-sheet to be mutagenized but only N- and/or C-terminal beta-sheets. Not only such guidance is absent in the specification, but it is also confusing in view of such instant claims as claims 5,6,11 directed to "at least two beta sheets", "three beta strands of two antiparallel beta sheets", "beta sheet in a domain or beta sheet in a subunit", respectively.

Further, applicant argues that amount of residues "on a surface of the protein" is very limited. No information about residues considered as being "on the surface" of gamma-globulin is present in the specification; in addition there is no definition of "a surface", and as any beta sheet of a protein is "a surface" and specification clearly addresses multiple beta sheets, and thus multiple surfaces, there is no sufficient guidance about which parts of which multiple beta strands of the multiple beta sheets are to be mutagenized. Examiner agrees that, for random mutagenesis, one would not need to know which amino acids need to be changed; however, in the absence of guidance for which parts of the "template molecule" are to be changed, with the insufficient guidance

Art Unit: 1631

and working examples and in view of unpredictability and the state of art, one skilled in the art could not make the invention with the claimed breadth without an undue amount of experimentation.

Conclusion

Claims 12,15 are objected as depending on rejected claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and rewritten to overcome the rejection under 35 U.S.C. § 112 .

Applicant's amendment necessitated the new/revised ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the date of this final action.

Art Unit: 1631

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michael Borin whose telephone number is (571) 272-0713. The examiner can normally be reached on 9am-5pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Marjorie Moran can be reached on (571) 272-0720. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.



Michael Borin, Ph.D.
Primary Examiner
Art Unit 1631